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pathway of S. fradiae (\$49054) (SEQ ID NO:116). Given in parentheses are protein accession numbers. The αβα fold with the NAD<sup>+</sup>-binding motif of GxGxxG is boxed.--

In accordance with 37 CFR §1.121 a marked up version of the above-amended paragraph(s) illustrating the changes introduced by the forgoing amendment(s) are provided in Appendix C.

## REMARKS

This amendment is provided in Response to the Notice to Comply With Requirements for Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant(s) request entry of this amendment in adherence with 37 C.F.R. §§1.821 to 1.825. This amendment is accompanied by a floppy disk containing the sequences (SEQ ID NOs:1-118) in computer readable form, and a paper copy of the sequence information that has been printed from the floppy disk.

The information contained in the computer readable form (floppy disk) was prepared through the use of the software program "PatentIn" and is identical to that of the paper copy.

This amendment contains no new matter. The amendments to the specification and/or claims are to provide a formal sequence listing and/or to provide appropriate cross-references to SEQ ID Numbers in accordance with 37 C.F.R. §§1.821 to 1.825. The sequence information provided herein finds support in the specification as filed.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510)-337-7871.

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Respectfully submitted,

Tom Hunter

Attorney for Applicant(s)

Reg. No: 38,498

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XPPENDIX A

## VERSION WITH MARKINGS TO SHOW CHANGES MADE IN 09/478,188 WITH ENTRY OF THIS AMENDMENT

## In the specification:

Table II at page 18:

Table II. C-1027 gene cluster open reading frames (27 to 42), primers for ORF amplification, a proposed functions

Position   Position	ORF	Relative	Primers	Function SEQ S	
Orf- 43945-46023 Fwd: GTG TGC CCG GTG ACA GAC, Antibiotic 71 27	0111		1		n
Rev: TCA GCC CAC GGC CTG GGA		(A	DNo:1)	10	
orf-         46167-47171         Fwd: GTG TTG GGC GAT GAG GAC Rev: TCA GAC CGC GGA CAT CTG methyltransfer ase         O-         73 methyltransfer ase           orf         47227-48485         Fwd: ATG GCC GGC CTG GTC ATG Rev: TCA GGA CCC GAG GGT CAC hydroxylase         76           29         Rev: TCA GGA CCC GAG GGT CAC hydroxylase         76           orf-         48610-49714         Fwd: GTG GAC CAG ACG TCT ACG Cyd GTG GTC GTC GTC GGT CAGG TGC AGG TGC AGG TGC AGG TGC AGG TGC GTC GTC GTC GTC GGT CGT CGT CGG CTC GTC G	orf-	43945-46023	Fwd: GTG TGC CCG GTG ACA GAC	Antibiotic 71	
Rev: TCA GAC CGC GGA CAT CTG	27	,D	Rev: TCA GCC CAC GGG CTG GGA	Transporter 72	
orf- 29	orf-	46167-47171	Fwd: GTG TTG GGC GAT GAG GAC	0- 73	
orf         47227-48485         Fwd: ATG GCC GGC CTG GTC ATG P450         75           29         Rev: TCA GGA CCC GAG GGT CAC hydroxylase         76           orf-         48610-49714         Fwd: GTG GAC CAG ACG TCT ACG Oxidoreductase         77           30         Rev: TCA TGC AGG TGC AGC GTG TC GTT CGG Unknown         79           31         Rev: TCA TCC CGG CCC GGC GGC GGC TAC TC	28		Rev: TCA GAC CGC GGA CAT CTG	methyltransfer 74	
Rev: TCA GGA CCC GAG GGT CAC				ase	
orf-         48610-49714         Fwd: GTG GAC CAG ACG TCT ACG Oxidoreductase         77           30         Rev: TCA TGC AGG TGC AGC GTG Orf-         78           orf-         50350-51390         Fwd: ATG AGG CCG CTC GTT CGG Unknown         79           31         Rev: TCA TCC CGG CCC GGC GGC Protein         80           orf-         51420-52341         Fwd: ATG AGA ACG CGG CGA CGC Oxidoreductase         81           32         Rev: TCA CGG CCG GAG GCG TAC Rev: TCA CGG CCG GAC TGT Unknown         83           33         Rev: CTA CTC ATT CCA GTT GTG Protein         84           orf-         54230-55379         Fwd: ATG TCT ACG GGC TAT CTC Unknown         85           34         Rev: TCA GCC GCC GCT GGC GCC Protein         86           orf-         56027-56881         Fwd: ATG TCT CC CCC GCC GCC DACG GCC DACG GCC DACG GCC CCC CCC GCC GCC CCC CCC GCC GCC	orf	47227-48485	Fwd: ATG GCC GGC CTG GTC ATG	-	
Rev: TCA TGC AGG TGC AGC GTG   78	29		Rev: TCA GGA CCC GAG GGT CAC	hydroxylase 76	
orf- 31         50350-51390 Rev:         Fwd: ATG AGG CCG CTC GTT CGG Rev:         Unknown         79 Protein           orf- 32         51420-52341 Rev:         Fwd: ATG AGA ACG CGG CGA CGC CCG GAG GCG TAC Rev:         Oxidoreductase         81 Rev:           32         Rev:         TCA CGG CCG GAG GCG TAC Rev:         B2 CTA CTC ATT CCA GTT GTG         Unknown         83 Rev:           33         Rev:         CTA CTC ATT CCA GTT GTG         Protein         84           orf- 34         Fwd:         ATG TCT ACG GGC TAT CTC         Unknown         85 Rev:         86 OTF- TCA GCC GCC GGT GGC GCC         Oxidase/ Protein         86 OTF- S6027-56881         Fwd:         ATG TTC TCC CCC GCC GCC         Oxidase/ OXIDANOWN         87           35         Rev:         TCA GTA CGC CTG GTG GGC TCC GGC GGC GGC GGC         Dehydrogenase         88 Unknown         89 Rev:           36         Rev:         TCA GCT CCC GGT CGC CGC         Dehydrogenase         88 Unknown         89           36         Rev:         TCA GCT CCC GGT CGC GCC         Protein         90           orf- 57834-58304         Fwd:         ATG ACC GCG ACG ACG ACC ACG GCC         Protein         90           orf- 578440-60091         Fwd:         ATG ACC GCG GCG GCG GCG GCG         92         Oxidoreductase         93 <td< td=""><td>orf-</td><td>48610-49714</td><td>Fwd: GTG GAC CAG ACG TCT ACG</td><td>Oxidoreductase 77</td><td></td></td<>	orf-	48610-49714	Fwd: GTG GAC CAG ACG TCT ACG	Oxidoreductase 77	
31         Rev:         TCA TCC CGG CCC GGC GGC         Protein         80           orf-         51420-52341         Fwd:         ATG AGA ACG CGG CGA CGC         Oxidoreductase         81           32         Rev:         TCA CGG CCG GAG GCG TAC         82           orf-         53241-54074         Fwd:         GTG TAT CAG CCG GAC TGT         Unknown         83           33         Rev:         CTA CTC ATT CCA GTT GTG         Protein         84           orf-         54230-55379         Fwd:         ATG TCT ACG GGC TAT CTC         Unknown         85           34         Rev:         TCA GCC GCC GGT GGC GCC         Protein         86           orf-         56027-56881         Fwd:         ATG TTC TCC CCC GCC GCC         Oxidase/         87           35         Rev:         TCA GTA CGC CTG GTG GGC         Dehydrogenase         88           orf-         56928-57730         Fwd:         ATG AAT TCG CTC GAC GAC         Unknown         89           36         Rev:         TCA GCT CCC GGT CGC         GC         Protein         90           orf-         57834-58304         Fwd:         ATG ACC GCG GCC GCC         ATC CT         Regulatory         91           37         Rev:         CTA	30		Rev: TCA TGC AGG TGC AGC GTG		
orf-         51420-52341         Fwd: ATG AGA ACG CGG CGA CGC         Oxidoreductase         81           32         Rev: TCA CGG CCG GAG GCG TAC         82           orf-         53241-54074         Fwd: GTG TAT CAG CCG GAC TGT         Unknown         83           33         Rev: CTA CTC ATT CCA GTT GTG         Protein         84           orf-         54230-55379         Fwd: ATG TCT ACG GGC TAT CTC         Unknown         85           34         Rev: TCA GCC GCC GCC GGC GCC         Protein         86           orf-         56027-56881         Fwd: ATG TTC TCC CCC GCC GCC         Oxidase/         87           35         Rev: TCA GTA CGC CTG GTG GGC         Dehydrogenase         88           orf-         56928-57730         Fwd: ATG AAT TCG CTC GAC GAC         Unknown         89           36         Rev: TCA GCT CCC GGT CGC CGC         Protein         90           orf-         57834-58304         Fwd: ATG ACC GCG GCG GCG CGC CGC         Protein         90           orf-         58440-60091         Fwd: ATG ACC GCG GCG CGC CGC         Protein         90           orf-         58440-60091         Fwd: ATG ACC CTG GAG GCC TAC         Regulatory         93           38         Rev: TCA GCC GCG GCG CGC CGC CGC         GCG CGC CGC CGC <td>orf-</td> <td>50350-51390</td> <td>Fwd: ATG AGG CCG CTC GTT CGG</td> <td>Unknown 79</td> <td></td>	orf-	50350-51390	Fwd: ATG AGG CCG CTC GTT CGG	Unknown 79	
32         Rev: TCA CGG CCG GAG GCG TAC         82           orf-         53241-54074         Fwd: GTG TAT CAG CCG GAC TGT         Unknown         83           33         Rev: CTA CTC ATT CCA GTT GTG         Protein         84           orf-         54230-55379         Fwd: ATG TCT ACG GGC TAT CTC         Unknown         85           34         Rev: TCA GCC GCC GGT GGC GCC         Protein         86           orf-         56027-56881         Fwd: ATG TCT CCC CGC GCC         Oxidase/         87           35         Rev: TCA GTA CGC CTG GTG GGC         Dehydrogenase         88           orf-         56928-57730         Fwd: ATG AAT TCG CTC GAC GAC         Unknown         89           36         Rev: TCA GCT CCC GGT CGC CGC         Protein         90           orf-         57834-58304         Fwd: ATG ACC GCG ACG AAT CCT         Regulatory         91           37         Rev: CTA GGC GGC GCG CGC GCG         Protein         90           orf-         58440-60091         Fwd: ATG AGC ACC ACG GCC GAG         Oxidoreductase         93           38         Rev: TCA GCC GCG CGC CGA CGG         94           orf-         60092-60622         Fwd: ATG ACC CTG GAG GCC TAC         Regulatory         95           39	31		Rev: TCA TCC CGG CCC GGC GGC	Protein 80	
orf-         53241-54074         Fwd: GTG TAT CAG CCG GAC TGT GTG Protein         Unknown 83           33         Rev: CTA CTC ATT CCA GTT GTG Protein         84           orf-         54230-55379         Fwd: ATG TCT ACG GGC TAT CTC Unknown 85         85           34         Rev: TCA GCC GCC GGT GGC GCC Protein 86         86           orf-         56027-56881         Fwd: ATG TTC TCC CCC GCC GCC Oxidase/ 87           35         Rev: TCA GTA CGC CTG GTG GGC Dehydrogenase 88           orf-         56928-57730         Fwd: ATG AAT TCG CTC GAC GAC Unknown 89           36         Rev: TCA GCT CCC GGT CGC CGC Protein 90           orf-         57834-58304         Fwd: ATG ACC GCG ACG AAT CCT Regulatory 91           37         Rev: CTA GGC GGC GCG TCC CGC GCG GCC GAG Oxidoreductase 93           38         Rev: TCA GCC GCG CGC CGA CGG GCC GAG GCC GAG GCC GAG GCC GAG GCC GAG GCC GAG GCC GCC	orf-	51420-52341	Fwd: ATG AGA ACG CGG CGA CGC	Oxidoreductase 81	
33         Rev: CTA CTC ATT CCA GTT GTG         Protein         84           orf-         54230-55379         Fwd: ATG TCT ACG GGC TAT CTC         Unknown         85           34         Rev: TCA GCC GCC GCC GCC GCC         Protein         86           orf-         56027-56881         Fwd: ATG TTC TCC CCC GCC GCC         Oxidase/         87           35         Rev: TCA GTA CGC CTG GTG GGC         Dehydrogenase         88           orf-         56928-57730         Fwd: ATG AAT TCG CTC GAC GAC         Unknown         89           36         Rev: TCA GCT CCC GGT CGC CGC         Protein         90           orf-         57834-58304         Fwd: ATG ACC GCG ACG AAT CCT         Regulatory         91           37         Rev: CTA GGC GGC GCG TCC CGC         92           orf-         58440-60091         Fwd: ATG AGC ACC ACG GCG GAG         Oxidoreductase         93           38         Rev: TCA GCC GCG CGC CGA CGG         94           orf-         60092-60622         Fwd: ATG ACC CTG GAG GCC TAC         Regulatory         95           39         Rev: TCA TGC GGG GCT CCC GGT         96           orf-         60940-62020         Fwd: GTG AAA AGT GAC TCT GCC         Regulatory         97	32		Rev: TCA CGG CCG GAG GCG TAC	82	
orf-         54230-55379         Fwd: ATG TCT ACG GGC TAT CTC         Unknown         85           34         Rev: TCA GCC GCC GGT GGC GCC         Protein         86           orf-         56027-56881         Fwd: ATG TTC TCC CCC GCC GCC         Oxidase/         87           35         Rev: TCA GTA CGC CTG GTG GGC         Dehydrogenase         88           orf-         56928-57730         Fwd: ATG AAT TCG CTC GAC GAC         Unknown         89           36         Rev: TCA GCT CCC GGT CGC CGC         Protein         90           orf-         57834-58304         Fwd: ATG ACC GCG ACG AAT CCT         Regulatory         91           37         Rev: CTA GGC GGC GGC GCG CGC         92           orf-         58440-60091         Fwd: ATG AGC ACC ACG GCC GAG         Oxidoreductase         93           38         Rev: TCA GCC GCG CGC CGA CGG         94           orf-         60092-60622         Fwd: ATG ACC CTG GAG GCC TAC         Regulatory         95           39         Rev: TCA TGC GGG GCT CCC GGT         96           orf-         60940-62020         Fwd: GTG AAA AGT GAC TCT GCC         Regulatory         97           40         Rev: TCA ACG GCG AGT TGG CTG         98           orf-         62045-62899         Fwd: GTG ACC	orf-	53241-54074	Fwd: GTG TAT CAG CCG GAC TGT	Unknown 83	
Rev: TCA GCC GCC GGT GGC GCC         Protein         86           orf-         56027-56881         Fwd: ATG TTC TCC CCC GCC GCC Oxidase/         87           35         Rev: TCA GTA CGC CTG GTG GGC Dehydrogenase         88           orf-         56928-57730         Fwd: ATG AAT TCG CTC GAC GAC Unknown         89           36         Rev: TCA GCT CCC GGT CGC CGC Protein         90           orf-         57834-58304         Fwd: ATG ACC GCG ACG AAT CCT Regulatory         91           37         Rev: CTA GGC GGC GCG TCC CGC         92           orf-         58440-60091         Fwd: ATG AGC ACC ACG GCC GAG Oxidoreductase         93           38         Rev: TCA GCC GCG CGC CGA CGG         94           orf-         60092-60622         Fwd: ATG ACC CTG GAG GCC TAC Regulatory         95           39         Rev: TCA TGC GGG GCT CCC GGT         96           orf-         60940-62020         Fwd: GTG AAA AGT GAC TCT GCC Regulatory         97           40         Rev: TCA ACG GCG AGT TGG CTG         98           orf-         62045-62899         Fwd: GTG ACC ACG AAC ACC ATC Regulatory         99           41         Rev: TCA CCC GCG ATC TCG ATC Regulatory         99           orf-         62788-63164         Fwd: (partial ORF)         p450	33		Rev: CTA CTC ATT CCA GTT GTG	Protein 84	
orf-         56027-56881         Fwd: ATG TTC TCC CCC GCC GCC Oxidase/         87           35         Rev: TCA GTA CGC CTG GTG GGC Dehydrogenase         88           orf-         56928-57730         Fwd: ATG AAT TCG CTC GAC GAC Unknown         89           36         Rev: TCA GCT CCC GGT CGC CGC Protein         90           orf-         57834-58304         Fwd: ATG ACC GCG ACG AAT CCT Regulatory         91           37         Rev: CTA GGC GGC GCG TCC CGC         92           orf-         58440-60091         Fwd: ATG AGC ACC ACG GCC GAG Oxidoreductase         93           38         Rev: TCA GCC GCG CGC CGA CGG         94           orf-         60092-60622         Fwd: ATG ACC CTG GAG GCC TAC Regulatory         95           39         Rev: TCA TGC GGG GCT CCC GGT         96           orf-         60940-62020         Fwd: GTG AAA AGT GAC TCT GCC Regulatory         97           40         Rev: TCA ACG GCG AGT TGG CTG         98           orf-         62045-62899         Fwd: GTG ACC ACG AAC ACC ATC Regulatory         99           41         Rev: TCA CCC GCG ATC TCG ATC         100           orf-         62788-63164         Fwd: (partial ORF)         p450         101	orf-	54230-55379	Fwd: ATG TCT ACG GGC TAT CTC	Unknown 85	
Rev: TCA GTA CGC CTG GTG GGC         Dehydrogenase         88           orf-         56928-57730         Fwd: ATG AAT TCG CTC GAC GAC Unknown         89           36         Rev: TCA GCT CCC GGT CGC CGC Protein         90           orf-         57834-58304         Fwd: ATG ACC GCG ACG AAT CCT Regulatory         91           37         Rev: CTA GGC GGC GCG TCC CGC         92           orf-         58440-60091         Fwd: ATG AGC ACC ACG GCC GAG Oxidoreductase         93           38         Rev: TCA GCC GCG CGC CGA CGG         94           orf-         60092-60622         Fwd: ATG ACC CTG GAG GCC TAC Regulatory         95           39         Rev: TCA TGC GGG GCT CCC GGT         96           orf-         60940-62020         Fwd: GTG AAA AGT GAC TCT GCC Regulatory         97           40         Rev: TCA ACG GCG AGT TGG CTG         98           orf-         62045-62899         Fwd: GTG ACC ACG AAC ACC ATC Regulatory         99           41         Rev: TCA CCC GCG ATC TCG ATC         100           orf-         62788-63164         Fwd: (partial ORF)         p450         101	34		Rev: TCA GCC GCC GGT GGC GCC	Protein 86	
orf-       56928-57730       Fwd: ATG AAT TCG CTC GAC GAC Unknown       89         36       Rev : TCA GCT CCC GGT CGC CGC Protein       90         orf-       57834-58304       Fwd: ATG ACC GCG ACG ACT CCT Regulatory       91         37       Rev: CTA GGC GGC GCG TCC CGC       92         orf-       58440-60091       Fwd: ATG AGC ACC ACG GCC GAG Oxidoreductase       93         38       Rev: TCA GCC GCG CGC CGA CGG       94         orf-       60092-60622       Fwd: ATG ACC CTG GAG GCC TAC Regulatory       95         39       Rev: TCA TGC GGG GCT CCC GGT       96         orf-       60940-62020       Fwd: GTG AAA AGT GAC TCT GCC Regulatory       97         40       Rev: TCA ACG GCG AGT TGG CTG       98         orf-       62045-62899       Fwd: GTG ACC ACG AAC ACC ATC Regulatory       99         41       Rev: TCA CCC GCG ATC TCG ATC       100         orf-       62788-63164       Fwd: (partial ORF)       p450       101	orf-	56027-56881	Fwd: ATG TTC TCC CCC GCC GCC		
36       Rev : TCA GCT CCC GGT CGC CGC       Protein       90         orf-       57834-58304       Fwd: ATG ACC GCG ACG ACG AAT CCT       Regulatory       91         37       Rev: CTA GGC GGC GCG TCC CGC       92         orf-       58440-60091       Fwd: ATG AGC ACC ACG GCC GAG       Oxidoreductase       93         38       Rev: TCA GCC GCG CGC CGA CGG       94         orf-       60092-60622       Fwd: ATG ACC CTG GAG GCC TAC       Regulatory       95         39       Rev: TCA TGC GGG GCT CCC GGT       96         orf-       60940-62020       Fwd: GTG AAA AGT GAC TCT GCC       Regulatory       97         40       Rev: TCA ACG GCG AGT TGG CTG       98         orf-       62045-62899       Fwd: GTG ACC ACG AAC ACC ATC       Regulatory       99         41       Rev: TCA CCC GCG ATC TCG ATC       100         orf-       62788-63164       Fwd: (partial ORF)       p450       101	35				
orf-       57834-58304       Fwd: ATG ACC GCG ACG AAT CCT       Regulatory       91         37       Rev: CTA GGC GGC GCG TCC CGC       92         orf-       58440-60091       Fwd: ATG AGC ACC ACG GCC GAG       Oxidoreductase       93         38       Rev: TCA GCC GCG CGC CGA CGG       94         orf-       60092-60622       Fwd: ATG ACC CTG GAG GCC TAC       Regulatory       95         39       Rev: TCA TGC GGG GCT CCC GGT       96         orf-       60940-62020       Fwd: GTG AAA AGT GAC TCT GCC       Regulatory       97         40       Rev: TCA ACG GCG AGT TGG CTG       98         orf-       62045-62899       Fwd: GTG ACC ACG AAC ACC ATC       Regulatory       99         41       Rev: TCA CCC GCG ATC TCG ATC       100         orf-       62788-63164       Fwd: (partial ORF)       p450       101		56928-57730			
37       Rev: CTA GGC GGC GCG TCC CGC       92         orf-       58440-60091       Fwd: ATG AGC ACC ACG GCC GAG       Oxidoreductase       93         38       Rev: TCA GCC GCG CGC CGA CGG       94         orf-       60092-60622       Fwd: ATG ACC CTG GAG GCC TAC       Regulatory       95         39       Rev: TCA TGC GGG GCT CCC GGT       96         orf-       60940-62020       Fwd: GTG AAA AGT GAC TCT GCC       Regulatory       97         40       Rev: TCA ACG GCG AGT TGG CTG       98         orf-       62045-62899       Fwd: GTG ACC ACG AAC ACC ATC       Regulatory       99         41       Rev: TCA CCC GCG ATC TCG ATC       Regulatory       99         orf-       62788-63164       Fwd: (partial ORF)       p450       101	36		Rev : TCA GCT CCC GGT CGC CGC	Protein 90	
orf-       58440-60091       Fwd: ATG AGC ACC ACG GCC GAG       Oxidoreductase       93         38       Rev: TCA GCC GCG CGC CGA CGG       94         orf-       60092-60622       Fwd: ATG ACC CTG GAG GCC TAC       Regulatory       95         39       Rev: TCA TGC GGG GCT CCC GGT       96         orf-       60940-62020       Fwd: GTG AAA AGT GAC TCT GCC       Regulatory       97         40       Rev: TCA ACG GCG AGT TGG CTG       98         orf-       62045-62899       Fwd: GTG ACC ACG AAC ACC ATC       Regulatory       99         41       Rev: TCA CCC GCG ATC TCG ATC       100         orf-       62788-63164       Fwd: (partial ORF)       p450       101	orf-	57834-58304	Fwd: ATG ACC GCG ACG AAT CCT		
38       Rev: TCA GCC GCG CGC CGA CGG       94         orf-       60092-60622       Fwd: ATG ACC CTG GAG GCC TAC       Regulatory       95         39       Rev: TCA TGC GGG GCT CCC GGT       96         orf-       60940-62020       Fwd: GTG AAA AGT GAC TCT GCC       Regulatory       97         40       Rev: TCA ACG GCG AGT TGG CTG       98         orf-       62045-62899       Fwd: GTG ACC ACG AAC ACC ATC       Regulatory       99         41       Rev: TCA CCC GCG ATC TCG ATC       100         orf-       62788-63164       Fwd: (partial ORF)       p450       101	37		Rev: CTA GGC GGC GCG TCC CGC		
orf-       60092-60622       Fwd: ATG ACC CTG GAG GCC TAC       Regulatory       95         39       Rev: TCA TGC GGG GCT CCC GGT       96         orf-       60940-62020       Fwd: GTG AAA AGT GAC TCT GCC       Regulatory       97         40       Rev: TCA ACG GCG AGT TGG CTG       98         orf-       62045-62899       Fwd: GTG ACC ACG AAC ACC ATC       Regulatory       99         41       Rev: TCA CCC GCG ATC TCG ATC       100         orf-       62788-63164       Fwd: (partial ORF)       p450       101	orf-	58440-60091	Fwd: ATG AGC ACC ACG GCC GAG		
39       Rev: TCA TGC GGG GCT CCC GGT       96         orf-       60940-62020       Fwd: GTG AAA AGT GAC TCT GCC       Regulatory       97         40       Rev: TCA ACG GCG AGT TGG CTG       98         orf-       62045-62899       Fwd: GTG ACC ACG AAC ACC ATC       Regulatory       99         41       Rev: TCA CCC GCG ATC TCG ATC       100         orf-       62788-63164       Fwd: (partial ORF)       p450       101	38		Rev: TCA GCC GCG CGC CGA CGG		
orf-       60940-62020       Fwd: GTG AAA AGT GAC TCT GCC       Regulatory       97         40       Rev: TCA ACG GCG AGT TGG CTG       98         orf-       62045-62899       Fwd: GTG ACC ACG AAC ACC ATC       Regulatory       99         41       Rev: TCA CCC GCG ATC TCG ATC       100         orf-       62788-63164       Fwd: (partial ORF)       p450       101	-	60092-60622		2	
40 Rev: TCA ACG GCG AGT TGG CTG 98 orf- 62045-62899 Fwd: GTG ACC ACG AAC ACC ATC Regulatory 99 41 Rev: TCA CCC GCG ATC TCG ATC 100 orf- 62788-63164 Fwd: (partial ORF) p450 101	39				
orf-       62045-62899       Fwd: GTG ACC ACG AAC ACC ATC Regulatory       99         41       Rev: TCA CCC GCG ATC TCG ATC       100         orf-       62788-63164       Fwd: (partial ORF)       p450       101		60940-62020		-	
41 Rev: TCA CCC GCG ATC TCG ATC 100 orf- 62788-63164 Fwd: (partial ORF) p450 101					
orf- 62788-63164 Fwd: (partial ORF) p450 101		62045-62899			
······································					
Rev: TCA CCT CGC CGT ACT CAC hydroxylase [102]		62788-63164		_	
	42		Rev: TCA CCT CGC CGT ACT CAC	hydroxylase [102]	

Page 6

Page 41, lines 3-25:

For type II PKS, the following two pairs of degenerate primers were used—5'-AGC TCC ATC AAG TCS ATG RTC GG-3' (forward, SEQ ID NO:102[103]) / 5'-CC GGT GTT SAC SGC GTA GAA CCA GGC G-3' (reverse, SEQ ID NO:103[104]) and 5'-GAC ACV GCN TGY TCB TCV-3' (forward, SEQ ID NO:104[105])/5'-RTG SGC RTT VGT NCC RCT-3' (SEQ ID NO:105[106]) (B, C+G+T; N, A+C+G+T; R, A+G; S, C+G; V, A+C+G; Y, C+T) (reverse) (Seow et al. (1997) J. Bacteriol., 179: 7360-7368). No product was amplified under all conditions tested. For type I PKS, the following pair of degenerate primers were used—5'-GCS TCC CGS GAC CTG GGC TTC GAC TC-3' (forward, SEQ ID NO:106[107]) / 5'-AG SGA SGA SGA GCA GGC GGT STC SAC-3' (S, G+C) (reverse, SEQ ID NO:107[108]) (Kakavas et al. (1997) J. Bacteriol., 179: 7515-7522). A distinctive product with the predicted size of 0.75 kb was amplified in the presence of 20% glycerol and cloned into pGEM-T according to the protocol provided by the manufacturer (Promega) to yield pBS1001.

For NGDH, the following pair of degenerate primers were used—5'-CS GGS GSS GCS GGS TTC ATC GG-3' (forward, SEQ ID NO:108[109]) / 5'-GG GWR CTG GYR SGG SCC GTA GTT G-3' (R, A+G; S, C+G; W, A+T; Y, C+T) (reverse, SEQ ID NO:109[110]) (Decker, et al. (1996) FEMS Lett., 141: 195-201). A distinctive product with the predicted size of 0.55 kb was amplified and cloned into pGEM-T to yield pBS1002.

For *cagA*, the following pair of primers, flanking its coding region, were used—5'-AG GTG GAG GCG CTC ACC GAG-3' (forward, SEQ ID NO:<u>110</u>[111])/5'-G GGC GTC AGG CCG TAA GAA G-3' (reverse, SEQ ID NO:<u>111</u>[112]) (Sakata *et al.* (1992) *Biosci. Biotechnol. Biochem.,* 56: 159201595). A distinctive product with the predicted size of 0.73 kb was amplified from pBS1005 and cloned into pGEM-T to yield pBS1003.

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--Figure 6 shows the DNA (SEQ ID NO:112) and deduced amino acid sequences of the 3.0-kb BamHI fragment from pBS1007, showing the sgcA (SEQ ID NO:113) and sgcB genes (SEQ ID NO:114). Possible RBSs are boxed. The presumed translational start and stop sites are in boldface. Restriction enzyme sites of interest are underlined. The amino acids, according to which the degenerated PCR primer were designed for amplifying the dNDP-glucose 4,6-dehydratase gene from S. globisporus, are underlined.

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Figure 7 shows the amino acid sequence alignment of SgcA (SEQ ID NO:113) with three other dNDP-glucose 4,6-dehydratases. Gdh, TDP-glucose 4,6-dehydratase of *S. erythraea* (AAA68211) (SEQ ID NO:115); MtmE, TDP-glucose 4,6-dehydratase in the mithramycin pathway of *S. argillaceus* (CAA71847) (SEQ ID NO:117); TylA2, TDP-glucose 4,6-dehydratase in the tylosin pathway of *S. fradiae* (S49054) (SEQ ID NO:116). Given in parentheses are protein accession numbers. The αβα fold with the NAD\*-binding motif of GxGxxG is boxed.--

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